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09/694,077	10/19/2000	Ilya Ravkin	VAI 301B	7890

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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/694,077	RAVKIN ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34 and 36-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34 and 36-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed May 26, 2006 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Status of the Claims

3. Claims 34-47 were pending. Applicants amended claims 34, 37 and 41. In addition, claim 35 was canceled. No claims were added. Therefore, claims 34 and 36-47 are currently pending and examined on the merits.

Withdrawn Objections/Rejections

4. The Lam et al. and Egner et al. rejection under 35 U.S.C. § 103(a) is withdrawn in view of Applicants amendment to claim 34. The objection to the specification is withdrawn in view of the amendments thereto. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 103

5. Claims 34, 36-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam et al. (Lam, K. S.; Salmon, S. E.; Hersh, E. M.; Hruby, V. J.; Kazmierski, W. M.; Knapp, R. J. "A

new type of synthetic peptide library for identifying ligand-binding activity" Nature **1991**, 354, 82-84) and Egner et al. (Egner, B. J.; Rana, S.; Smith, H.; Bouloc, N.; Freg, J. G.; Brocklesby, W. S.; Bradley, M. "Tagging in combinatorial chemistry: the use of coloured and fluorescent beads" Chem. Commun., **1997**, 735-736) and Lee (U.S. Patent No. 4,053,433) (Date of Patent is **1977**) and Blawas et al (Blawas, A.S.; Reicher, W. M. "Protein Patterning" Biomaterials **1998** *19*, 595-609) and Noonan et al (U.S. Patent No. 6,129,896) (Filing Date is **December 17, 1998**) and Walt (U.S. Patent No. 6,210,910) (Filed **March 2, 1998**).

For ***claims 34 and 41***, Lam et al. (see entire document) teach a method for identifying ligand-binding activity using a synthetic 'one-bead, one-peptide' approach (e.g., see abstract), which reads on the claimed invention. For example, Lam et al. disclose providing a first class of particles in a first reaction vessel and a second class of particles in a second reaction vessel wherein a first type of analyte is attached to said first class of particles and a second type of analyte is attached to said second class of particles (e.g., see page 82, column 1, last paragraph, "The first cycle consisted of distributing a pool of resin beads into separate reaction vessels each with a single amino acid [i.e., different class of analyte]"; see also figure 1, wherein the first class = A, second class = G, etc. and each class is in its own reaction vessel; see also page 82, column 2, paragraph 3 describing formation of pentapeptide library with ~2,476,099 members). Lam et al. also disclose forming a mixture of particles from the first and second vessels, the mixture having substantially equal numbers of particles for each vessel (e.g., see figure 1, "randomization" step; see also page 82, column 1, last paragraph, "Our method involves creating a large peptide library ... representing the universe of possible random peptides

in roughly equimolar proportion"). Lam et al. further disclose dispersing a portion of the mixture to an examination site on a surface, the particles of the first and second classes being distributed to random positions across the examination site (e.g., see figure 2; see also page 82, column 2, paragraph 1). Lam et al. further disclose reacting the portion of the mixture with a test substance such as a labeled antibody against β-endorphin or streptavidin (e.g., see Tables 1 and 2; see also figure 2). Lam et al. also disclose acquiring at least one image of particles at the examination site on the surface (e.g., see figure 2 showing low- and high-power photomicrographs).

For ***claims 39 and 46***, Lam et al. disclose covalent attachment of pentapeptide sequences (e.g., see figure 1; see also abstract).

For ***claims 40 and 47***, Lam et al. disclose a reaction step that occurs before the dispensing step (e.g., see Lam et al., page 82, column 2, paragraph 1, "Acceptor molecules were ... added in soluble form to the peptide-bead library [i.e., before analysis]"). Also note that optimization of process steps, especially with respect to ordering, is within the routine skill of the art. *In re Burhans*, 154 F.2d 690, 69 USPQ330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results).

Lam et al. differ from the claimed invention as follows:

For ***claims 34 and 42***, Lam et al. fail to teach the use of a first and second optically detectable code to interpret the result of such a binding experiment. In addition, Lam et al. only teach the use instead labels such as alkaline phosphatase coupled with various sequencing techniques to identify petapeptides that interact with the ligands. In

addition, Lam et al. fail to teach at least one flat viewing surface and a shape that self-orients the viewing surface to face a viewing direction substantially perpendicular to the surface. Lam et al. only teach the use of round beads.

For ***claims 36 and 43***, Lam et al. fail to teach each particle has at least one transparent portion.

For ***claims 37 and 44***, Lam et al. fail to teach carriers as a combination of fused fibers of various colors, the colors and relative positions of the fibers indicating the code.

For ***claim 38 and 45***, Lam et al. fail to teach the attachment of biological cells to the particles for cell identification. The combined references of Lam et al. and Egner et al. only teach the use of peptides.

For ***claim 41***, Lam et al. fail to teach the additional steps of acquiring a set of images of particles at the examination site, each image corresponding to a different spectral band an operating via the use of a computer program to identify particles of the same class by using the images to develop a mask for the particles of the same class, and detecting one or more reporting modalities within the mask. The combined references of Lam et al. and Egner et al. only disclose imagining different spectral bands and the use of filter masks (e.g., see figures 1 and 2), but the references is silent as to whether a "computer" program takes advantage of these measurements for identification.

However, the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. teach the following limitations that are deficient in Lam et al. and Egner et al.:

For ***claims 34 and 42***, the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. (see entire documents) teach the use of a first and second class of detectable codes to aid in the identification of a library of peptides bound to beads (e.g., see Egner et al., figures 1 and 4; see also Footnotes disclosing that various dyes can be used to label each "class" of library member, for example, pyrene butanoic acid = Val, methyl red = Ala, etc.). In addition, the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. teach that the microcarriers can have generally a flat shape with two substantially parallel planar sides instead of the round shape of a bead (e.g., see Lee, figures 2-5 disclosing examples of a planar "top" and a planar "bottom" side that are substantially parallel and flat; see also lines 37-38 showing that these taggants are useful for producing "libraries" like the libraries disclosed by Lam et al.; see also Noonan et al, figures 3 and 4; see also column 2, lines 23-26; see also column 2, last three paragraphs, "Method 100 begins by synthesizing functional moieties onto a plurality of fibers ... For example, functional moieties may include DNA oligonucleotides for DNA testing biosensor devices. Alternative, the functional moieties may include proteins, peptide, Antibodies"; see also figure 2; see also Blawas et al, pages 605-606, section 4.3, wherein Blawas et al disclose that bound proteins and/or antibodies can be used to control the areas of cell adhesion and/or growth to a substrate surface i.e., the cells bind to the proteins that are attached to the fused glass and/or plastic chips).

For ***claims 36 and 43***, the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. teach a transparent portion (e.g., see Lee, column 3, lines 60-62, "A list of suitable colors may include: Clear").

For ***claims 37 and 44***, the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. teach fused colored fibers wherein said fibers represent the code (e.g., see Lee, figures 2-5, see also column abstract, see also column 2, Summary of Invention, wherein the code is detectable on either planar side; see also column 4, lines 49-52, "A preferred type of color-coded microparticle ... consists of microscopic pieces of colored plastic films fused together to form a rectangular 'microsandwich'"; see also column 4, lines 46-48; see also, column 2, line 46 disclosing 233,846,052 uniquely coded batches of microcarriers; see also see figure 5 disclosing fused fibers).

For ***claims 38 and 45***, the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. teach the attachment of biological cells to the particles for cell identification. For example, Noonan et al and Blawas et al teach the use of fused glass and/or plastic fibers can be cut into chips and used as biosensors to attach biological cells (e.g., see Noonan et al, column 2, lines 23-26; see also column 2, last three paragraphs, "Method 100 begins by synthesizing functional moieties onto a plurality of fibers ... For example, functional moieties may include DNA oligonucleotides for DNA testing biosensor devices. Alternative, the functional moieties may include proteins, peptide, Antibodies"; see also Blawas et al, pages 605-606, section 4.3, wherein Blawas et al disclose that bound proteins and/or antibodies can be used to control the areas of cell adhesion and/or growth to a substrate surface i.e., the cells bind to the proteins that are attached to the fused glass and/or plastic chips).

For ***claim 41***, the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. teach the use of a computerized sensor array for randomly detecting

a mixed population of sells wherein each individual cell in the are is positioned in an optically addressable microwell (e.g., see Walt et al., abstract; see also column 5, lines 57 through column 6, line 20; see also column 7, lines 24-40; see also figures 1 and 3; see also column 12, lines 59-65). Each cell population is individually encoded with a single fluorophores or chromophore or ratios of such dyes like the as was disclosed by Egner et al. (e.g., see Walt et al., column 7, lines 24-40; column 15, lines 15 through column 20, lines 31; column 19, line 66 though column 20, line 11) and the identity and location of each cell type is determined by the characteristic optical response signature of the fluorophores or chromophore dye or ratios of such dyes (e.g., see Walt et al., column 15, lines 25-42; column 16, lines 18-26; column 20, lines 12-31). The type of cell includes adipocyte fat cells, neurons, and fibroblasts. The apparatus for the optical detection of the cells includes instruments such as epifluorescence microscope and CCD camera and the data is processed by a computer using an image processing software (e.g., see Walt et al., column 26, lines 28-55).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make to use the colored and fluorescently labeled beads as disclosed by Egner et al. to make the peptide library as disclosed by Lam et al. for the purposes of facile high throughput screening because Egner et al. explicitly state that their labeled beads were created for this purpose and further use the embodiments disclosed in the Lam et al. reference as an example (e.g., see Egner et al., page 736, paragraph bridging columns 1-2, "The use of colored and fluorescent beads has the potential, we believe, to simplify the identification of library members for single bead

screening application"; see also page 735, column 1, paragraph 3, wherein the Lam et al. article is explicitly cited in footnote number 2). Furthermore, one of ordinary skill in the art would have been motivated to use the colored and labeled beads as taught by Egner et al. because according to Egner et al. it is a "simple" technique that is "non-destructive" and "very sensitive, with detection levels easily down to femtomoles of material/bead" (e.g., see Egner, et al., page 736, column 1, last paragraph). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Egner et al. actually use the method of Lam et al. to synthesize their library (e.g., see Egner et al, page 735, column 1, paragraph 3 wherein the Lam et al. reference is cited for the library preparation in footnote 2).

In addition to the spherical beads disclosed by the combined teachings of Lam et al. and Egner et al. (as set forth above) other shapes and/or carriers (including carriers that have at least one flat viewing surface and a shape that self-orients the viewing surface to face a viewing direction) would also have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. For example, the combined references of Lee, Blawas et al., Noonan et al., and Walt et al. teach the use of various other carriers that were standard in the art at the time the invention was made including the use of flat fused fibers made of glass and/or plastic that will "self-orient" to place the flat surface in the viewing direction (e.g., see Lee, abstract expressly stating that their taggants can be used to label chemicals; see also figures 2-6; see also column 2, lines 37 and 38 wherein Lee expressly state that these taggants are useful for the production of "libraries", which would encompass the libraries produced by Lam et al.; see also column

1, lines 57 wherein the screening of "proteinaceous" materials is disclosed i.e., like the "proteinaceous" peptide libraries disclosed by Lam et al.; see also Noonan et al., figure 3; see also column 2, lines 60-63 stating that similar fused fibers can be used to "attach" a wide variety of ligands including proteins, antibodies, nucleic acids, etc.). Furthermore, a person of ordinary skill in the art would have been motivated to use the fused fibers as disclosed by the combined reference of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. to replace the spherical carriers as disclosed by the combined teachings of Lam et al. and Egner et al. because Noonan et al., for example, state that these fused fiber carriers are easy to make, cheap to produce and can be monitored using "cleavable linkers" for better "quality control" (e.g., see Noonan et al., column 2, paragraph 1). In addition, Lee, demonstrates that an enormous number of codes can be generated using similar fused fibers (e.g., taggants), which is exactly what is required for labeling combinatorial libraries (e.g., see Lee, column 2, lines 22-23, see also lines 28-45, "The improvement ... comprises providing microparticles ... [that] are encoded according to, a particular orderly sequence of visually color distinguishable dyed and/or pigmented layers ... For example, using a library of 12 colors in an eight-membered sequence, wherein no color is used adjacent to itself, the number of codes would be determined as follows ... this system includes 233,846,052 possible codes"). Finally, a person of skill in the art would reasonably have been expected to be successful because the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. disclose that proteins, peptides, nucleic acids, and antibodies can all be easily attached to these carriers just like Lam et al. and Egner et al. demonstrated that peptides could be easily attached to

the spherical beads (see Noonan et al., column 2, second to last paragraph; see also figure 2 showing standard synthesis procedures for connecting peptides, proteins, nucleic acids etc. to the glass, plastic, polymer, etc. solid supports). In addition, both Lee and Noonan et al. disclose the same bundled and/or fused fibers made of glass, plastic and/or polymers (e.g., see Noonan et al., abstract; see also Summary of the Invention disclosing fused and/or bundled fibers; see also claims 16 and 17 disclosing plastic and glass; see also Lee, Example 1 disclosing bundled and/or fused fibers; see also figures 1-6; see also column 4, last two paragraphs; see also column 3, lines 25-40 disclosing plastic and glass). Furthermore, both Lee, like Lam et al., also disclose the use of a microscope to analyze the carriers, which would encompass the microscopic techniques disclosed by the combined references of Egner et al. and Lam et al. (e.g., see Lee, column 1, line 32; see also Summary of the Invention). In addition, both Noonan et al. and Lam et al. indicate that peptides, proteins, antibodies and nucleic acids like RNA can be screened (e.g., compare Noonan et al., column 2, lines 59-61 to Lam et al., page 82, column 2, paragraph 1).

Furthermore, it would also have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the carriers, including fused glass and/or plastic fibers, as taught by the combined references of Lee, Lam et al., Egner et al. and Noonan et al. (see above), for the purpose of tagging cells because the combined references of Noonan et al., Blawas et al. and Walt et al., for example, explicitly state teach that fused glass fibers can be used for this purpose (e.g., see Noonan et al., abstract, column 2, Summary of the Invention; see also Blawas et al., page 605-606, section 4.3;

see also Background of the invention and Table 1). A person of skill in the art would have been motivated to use the color coded fused glass and/or plastic as biosensors for detecting cells because Noonan et al., for example, explicitly state that the use of bundled fibers are a "preferred embodiment" (e.g., see column 2, paragraph 2, "the bonded fiber"; see also column 2, last two paragraphs, see also column 1, paragraph 2). Furthermore, Blawas et al. disclose that immobilized biomolecules can be beneficially used to monitor cell adhesion and/or growth (e.g., see entire document, especially, section 4.3 and figure 5). In addition, Walt et al. disclose that their sensors offer "distinct advantages" for high throughput screening of combinatorial libraries including the evaluation of hundreds of thousands of candidate compounds and, in addition, is particularly useful for screening cells using single or mixed dyes (e.g., see Walt et al., Summary of Invention). One of ordinary skill in the art would have reasonably expected to be successful because Blawas et al., Noonan et al. and Lee all separately disclose that fused glass and/or plastic can be used to label cells (e.g., see Blawas et al., Table I, Substrate column; see also Noonan et al., column 3, line 1; see also Lee, column 4, line 51). Furthermore, a person of skill in the art would have reasonably expected to be successful using the sensor as disclosed by Walt et al. because Walt et al. teach that both single fluorophoric or chromophoric dye can be used for encoding the cells or, in an alternative embodiment, two or more encoding materials or dyes may be used to encode cell populations and the optical response intensity ratios for the dyes, produced by exposure to excitation light energy, are employed to encode and identify members of the cell population with the array, which would encompass the methods of Egner et al.

Response

6. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue that there is no motivation to combine the references and no expectation of success (e.g., see 5/26/06 Response, pages 9-11).

[2] Applicants state that Lee is (1) directed to tagging "bulk" materials such as grains and chemicals, (2) used only in "trace" amounts, and (3) not "attached to" the chemicals and, as a result, "does not teach or suggest the use of microparticles to support or carry attached analytes" (e.g., see 5/26/06 Response, paragraph bridging pages 11 and 12).

[3] Applicants argue, "Lee teaches away from such use by suggesting conditions ... that reduce or minimize attachment, even incidental attachment" (e.g., see 5/26/06 Response, page 12, paragraph 1).

[4] Applicants argue that impermissible hindsight has been used (e.g., see 5/26/06 Response, page 12, last paragraph).

This is not found persuasive for the following reasons:

[1] In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some

teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one of ordinary skill in the art would have been motivated to use the colored and labeled beads as taught by Egner et al. because according to Egner et al. it is a "simple" technique that is "non-destructive" and "very sensitive, with detection levels easily down to femtomoles of material/bead" (e.g., see Egner, et al., page 736, column 1, last paragraph). In addition, Furthermore, a person of ordinary skill in the art would have been motivated to use the fused fibers as disclosed by the combined reference of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. to replace the spherical carriers as disclosed by the combined teachings of Lam et al. and Egner et al. because Noonan et al., for example, state that these fused fiber carriers are easy to make, cheap to produce and can be monitored using "cleavable linkers" for better "quality control" (e.g., see Noonan et al., column 2, paragraph 1). In addition, Lee, demonstrates that an enormous number of codes can be generated using similar fused fibers (e.g., taggants), which is exactly what is required for labeling combinatorial libraries (e.g., see Lee, column 2, lines 22-23, see also lines 28-45, "The improvement ... comprises providing microparticles ... [that] are encoded according to, a particular orderly sequence of visually color distinguishable dyed and/or pigmented layers ... For example, using a library of 12 colors in an eight-membered sequence, wherein no color is used adjacent to itself, the number of codes would be determined as follows ... this system includes 233,846,052 possible codes"). Furthermore, Blawas et al. also disclose that immobilized biomolecules can be beneficially used to monitor cell adhesion and/or growth (e.g., see entire document, especially, section 4.3 and figure 5). In

addition, Walt et al. disclose that their sensors offer "distinct advantages" for high throughput screening of combinatorial libraries including the evaluation of hundreds of thousands of candidate compounds and, in addition, is particularly useful for screening cells using single or mixed dyes (e.g., see Walt et al., Summary of Invention).

Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Egner et al. actually use the method of Lam et al. to synthesize their library (e.g., see Egner et al, page 735, column 1, paragraph 3 wherein the Lam et al. reference is cited for the library preparation in footnote 2). In addition, a person of skill in the art would reasonably have been expected to be successful because the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. disclose that proteins, peptides, nucleic acids, and antibodies can all be easily attached to these carriers just like Lam et al. and Egner et al. demonstrated that peptides could be easily attached to the spherical beads (see Noonan et al., column 2, second to last paragraph; see also figure 2 showing standard synthesis procedures for connecting peptides, proteins, nucleic acids etc. to the glass, plastic, polymer, etc. solid supports). In addition, both Lee and Noonan et al. disclose the same bundled and/or fused fibers made of glass, plastic and/or polymers (e.g., see Noonan et al., abstract; see also Summary of the Invention disclosing fused and/or bundled fibers; see also claims 16 and 17 disclosing plastic and glass; see also Lee, Example 1 disclosing bundled and/or fused fibers; see also figures 1-6; see also column 4, last two paragraphs; see also column 3, lines 25-40 disclosing plastic and glass). Furthermore, both Lee, like Lam et al., also disclose the use of a microscope to analyze the carriers, which would encompass the microscopic techniques disclosed by the combined references of Egner et al. and Lam et al. (e.g., see Lee, column 1, line 32; see also Summary of

the Invention). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Blawas et al., Noonan et al. and Lee all separately disclose that fused glass and/or plastic can be used to label cells (e.g., see Blawas et al., Table I, Substrate column; see also Noonan et al., column 3, line 1; see also Lee, column 4, line 51).

[2] In response to applicant's arguments against the Lee reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, the "combination" of references clearly suggests the use of microparticles, including fused fibers, to support or carry attached analytes. For example, the combined references of Lee, Blawas et al., Noonan et al., and Walt et al. teach the use of various other carriers that were standard in the art at the time the invention was made including the use of flat fused fibers made of glass and/or plastic that will "self-orient" to place the flat surface in the viewing direction (e.g., see Lee, abstract expressly stating that their taggants can be used to label chemicals; see also figures 2-6; see also Noonan et al., figure 3; see also column 2, lines 60-63 stating that similar fused fibers can be used to "attach" a wide variety of ligands including proteins, antibodies, nucleic acids, etc.). Furthermore, a person of ordinary skill in the art would have been motivated to use the fused fibers as disclosed by the combined reference of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. to replace the spherical carriers as disclosed by the combined teachings of Lam et al. and Egner et al. because Noonan et al., for example, state that these fused fiber carriers are easy to make, cheap to produce and can be monitored using "cleavable linkers" for better "quality control" (e.g., see Noonan et al., column 2, paragraph 1). In addition, Lee, demonstrates

that an enormous number of codes can be generated using similar fused fibers (e.g., taggants), which is exactly what is required for labeling combinatorial libraries (e.g., see Lee, column 2, lines 22-23, see also lines 28-45, "The improvement ... comprises providing microparticles ... [that] are encoded according to, a particular orderly sequence of visually color distinguishable dyed and/or pigmented layers ... For example, using a library of 12 colors in an eight-membered sequence, wherein no color is used adjacent to itself, the number of codes would be determined as follows ... this system includes 233,846,052 possible codes"). Finally, a person of skill in the art would reasonably have been expected to be successful because the combined references of Lee, Egner et al., Blawas et al., Noonan et al., and Walt et al. disclose that proteins, peptides, nucleic acids, and antibodies can all be easily attached to these carriers just like Lam et al. and Egner et al. demonstrated that peptides could be easily attached to the spherical beads (see Noonan et al., column 2, second to last paragraph; see also figure 2 showing standard synthesis procedures for connecting peptides, proteins, nucleic acids etc. to the glass, plastic, polymer, etc. solid supports).

[3] "[A] reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be lead in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend upon the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994) (citing *United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 478, 484 (1966)). Here, there is no express language in the Lee reference that would

"discourage" a person of ordinary skill in the art from attaching analytes to the microparticles. Contrary to Applicants' implications, the Lee reference never makes a statement like "attachment of analytes to the microparticles is forbidden." The passages cited by Applicants (e.g., column 6, lines 1-6) merely refer to a preferred embodiment (e.g., see column 5, last paragraph, "The method of the present invention is particularly well suited for the tagging of bulk materials [i.e., tagging bulk materials is simply a preferred embodiment]"; see also abstract which does not limit the teachings of the reference to "bulk" materials) and it is well established that preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See MPEP § 2123. Here, the Lee reference discloses a broad teaching for making combinatorial libraries in general (e.g., see column 2, lines 37-38; see also column 1, line 57 disclosing as an example a use for labeling proteinaceous materials like the polypeptide libraries disclosed by Lam et al.).

In addition, a reference that "teaches away" does not *per se* preclude a *prima facie* case of obviousness, but rather the "teaching away" of the reference is a factor to be considered in determining unobviousness. Id 27 F.3d at 552, 31 USPQ 2d at 1132. Here, Noonan et al. (e.g., see rejection above), for example, expressly state that fused and/or bundled fibers (like the ones disclosed by Lee) can be used for the "attachment" of analytes. This fact alone would outweigh any alleged teaching away by Lee even if, *assuming arguendo*, the Lee reference could be fairly interpreted in this fashion (which is not the case). In addition, the Examiner's position is further supported by the general state of the prior art (e.g., as exemplified by Main et al.), which proves that libraries, including peptide libraries (like the peptide libraries set forth by Lam et al., Egner et al., etc.), were routinely synthesized using a wide variety of shapes and/or materials including

"beads, pellets, discs, capillaries, hollow fibers, needles, solid fibers" made from "cellulose, pore-glass, silica gel, polystyrene resin, [etc.]" (e.g., see Main et al., page 3, last full paragraph). According to Main et al., a solid support just has to be "inert" and "mechanically stable" (e.g., see Main et al., page 3, last full paragraph), which is exactly what Lee, Noonan et al., etc. disclose (e.g., see Lee, column 5, last paragraph showing that these solid supports can even survive a dynamite blast if necessary).

[4] In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As stated above (see sections **[1]-[3]**), the rejection takes into account only knowledge that was within the level of ordinary skill at the time the claimed invention was made.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

Additional References Illustrative of the State of Prior Art

Main et al. (WO 97/03931) (February 6, 1997) demonstrate that libraries, including peptide libraries (like those disclosed by Lam et al., Egner et al., etc.), were routinely synthesized using a wide variety of shapes and/or materials including "beads, pellets, discs, capillaries, hollow fibers, needles, solid fibers" made from "cellulose, pore-glass, silica gel, polystyrene resin, [etc.]" (e.g.,

see Main et al., page 3, last full paragraph). According to Main et al., a solid support just has to be "inert" and "mechanically stable" (e.g., see Main et al., page 3, last full paragraph).

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
August 2, 2006

JON EPPERSON, PH.D.
PATENT EXAMINER